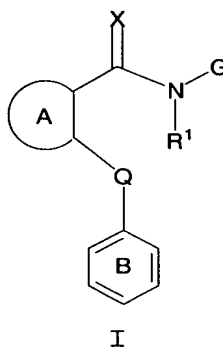


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We claim:

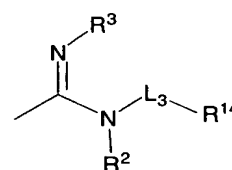
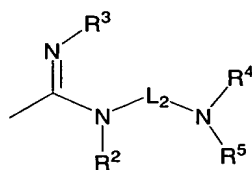
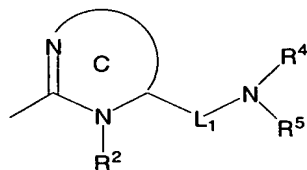
1. A compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

X is oxygen or sulfur;

G is G1, G2 or G3:



Ring C of G1 is an optionally substituted 5-6 membered aromatic or non-aromatic ring having two or three ring nitrogens;

L_1 is a C_{1-6} alkylidene chain optionally substituted by 1-3 R^6 , wherein the alkylidene chain is optionally interrupted by $-C(R^{11})_2-$, $-C(R^{11})_2C(R^{11})_2-$, $-C(R^{11})=C(R^{11})-$, $-C\equiv C-$, $-O-$, $-S-$, $-N(R^1)$, $-N(R^{10})CO-$, $-N(R^{10})CO_2-$, $-CON(R^{10})-$, $-C(R^{11})(OR^1)-$, $-CO-$, $-CO_2-$, $-OC(=O)-$, $-OC(=O)N(R^{10})-$, $-SO-$, $-SO_2-$, $-N(R^{10})SO_2-$, or $-SO_2N(R^{10})-$, and wherein L_1 or a portion thereof optionally forms part of a 3-7 membered ring;

L_2 is a C_{2-6} alkylidene chain optionally substituted by 1-3 R^6 , wherein the alkylidene chain is optionally interrupted by

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- $-C(R^{11})_2-$, $-C(R^{11})_2C(R^{11})_2-$, $-C(R^{11})=C(R^{11})-$, $-C\equiv C-$, $-O-$, $-S-$,
 $-N(R^{11})_2-$, $-N(R^{10})CO-$, $-N(R^{10})CO_2-$, $-CON(R^{10})-$, $-C(R^{11})(OR^1)-$,
 $-CO-$, $-CO_2-$, $-OC(=O)-$, $-OC(=O)N(R^{10})-$, $-SO-$, $-SO_2-$, $-$
 $N(R^{10})SO_2-$ or $-SO_2N(R^{10})-$, and wherein L_2 or a portion
5 thereof optionally forms part of a 3-7 membered ring;
 L_3 is a direct link, a C_{1-6} alkylidene chain optionally
substituted by 1-3 R^6 , wherein the alkylidene chain is
optionally interrupted by $-C(R^{11})_2-$, $-C(R^{11})_2C(R^{11})_2-$,
 $-C(R^{11})=C(R^{11})-$, $-C\equiv C-$, $-O-$, $-S-$, $-N(R^{11})$, $-N(R^{10})CO-$,
10 $-N(R^{10})CO_2-$, $-CON(R^{10})-$, $-C(R^{11})(OR^1)-$, $-CO-$, $-CO_2-$,
 $-OC(=O)-$, $-OC(=O)N(R^{10})-$, $-SO-$, $-SO_2-$, $-N(R^{10})SO_2-$, or
 $-SO_2N(R^{10})-$, and wherein L_3 or a portion thereof optionally
forms part of a 3-7 membered ring;
 R^1 is hydrogen or C_{1-6} aliphatic;
15 each R^2 is independently selected from hydrogen, C_{1-8}
aliphatic, C_{6-10} aryl, C_{7-10} aralkyl, or, when Ring C is a
6-membered aromatic ring R^2 is a lone electron pair;
 R^3 is hydrogen, C_{1-8} aliphatic, C_{6-10} aryl, or C_{7-10} aralkyl;
 R^4 is hydrogen, C_{1-8} aliphatic, $C=O(C_{1-8}$ aliphatic), $CO_2(C_{1-8}$
20 aliphatic), $C(=O)N(R^{10})(C_{1-7}$ aliphatic), C_{6-10} aryl,
heteroaryl, C_{7-12} aralkyl, or heteroaralkyl;
 R^5 is hydrogen or C_{1-8} aliphatic, or R^4 and R^5 taken together
with their intervening nitrogen form a substituted or
unsubstituted, aromatic or non-aromatic, 4-14 membered
25 monocyclic, bicyclic or tricyclic ring system having, in
addition to said intervening nitrogen, 0-4 ring
heteroatoms selected from nitrogen, sulfur or oxygen;
Ring A is a 5-membered heteroaryl ring or a 6-membered
aromatic ring having 0-2 ring nitrogen atoms, wherein Q
30 and $C(=X)N(R^1)-G$ are attached at ortho positions on Ring A
and wherein Ring A is optionally substituted by one to
three R^7 ;

Ring B is a 6-membered aromatic ring having 0-2 ring nitrogen atoms, wherein Ring B is optionally substituted by one or more R⁸;

Q is a C₂-C₄ alkylidene chain optionally substituted by one
5 to three R⁹, wherein a methylene unit of the alkylidene chain is optionally replaced by -S-, -S(O)-, -SO₂-, -N(R¹)-, -O-, -C(O)-, or -C(S)-;

each R⁶ is independently selected from halo, -OR¹, -CN, -C₁₋₆ aliphatic, -N(R¹⁰)₂, -C=O(C₁₋₅ aliphatic), -CO₂R¹, -CH₂CO₂R¹,
10 or -C(=O)N(R¹⁰)(C₁₋₅ aliphatic);

each R⁷ is independently selected from -halo, -NO₂, -CN, or a substituted or unsubstituted group selected from -R¹², -OR¹, -SR¹², -C₆₋₁₀ aryl, -heterocyclyl, -heteroaryl, -(C₆₋₁₀ aryl)alkyl, -(heterocyclyl)alkyl, -(heteroaryl)alkyl,
15 -N(R¹⁰)₂, -NR¹⁰C(O)R¹, -NR¹⁰C(O)N(R¹⁰)₂, -NR¹⁰CO₂R¹², -CO₂R¹, -C(O)R¹, -C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -S(O)₂R¹², -SO₂N(R¹⁰)₂, -S(O)R¹², -NR¹⁰SO₂N(R¹⁰)₂, -NR¹⁰SO₂R¹², or -C(=NH)-N(R¹⁰)₂, or two adjacent R⁷ taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated
20 ring having 0-2 ring heteroatoms selected from nitrogen, oxygen or sulfur;

each R⁸ is independently selected from -halo, -NO₂, -CN, or a substituted or unsubstituted group selected from -R¹², -OR¹, -SR¹², -C₆₋₁₀ aryl, -heterocyclyl, -heteroaryl, -(C₆₋₁₀ aryl)alkyl, -(heterocyclyl)alkyl, -(heteroaryl)alkyl,
25 -N(R¹⁰)₂, -NR¹⁰C(O)R¹, -NR¹⁰C(O)N(R¹⁰)₂, -NR¹⁰CO₂R¹², -CO₂R¹, -C(O)R¹, -C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -S(O)₂R¹², -SO₂N(R¹⁰)₂, -S(O)R¹², -NR¹⁰SO₂N(R¹⁰)₂, -NR¹⁰SO₂R¹², or -C(=NH)-N(R¹⁰)₂, or two adjacent R⁸ taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated
30 ring having 0-2 ring heteroatoms selected from nitrogen, oxygen or sulfur;

each R^9 is independently selected from halo, OR^1 , CN, C_{1-6} aliphatic, $N(R^{10})_2$, $C=O(C_{1-5}$ aliphatic), $CO_2(C_{1-5}$ aliphatic), or $C(=O)N(R^{10})(C_{1-5}$ aliphatic), or R^9 and an R^7 , at a position ortho to Q, are taken together with their intervening
5 atoms form a 5-7 membered unsaturated or partially unsaturated ring having 0-2 ring heteroatoms selected from N, O or S;

each R^{10} is independently selected from hydrogen, a substituted or unsubstituted C_{1-8} aliphatic group, $C(=O)R^1$,
10 CO_2R^1 , SO_2R^1 , or two R^{10} on the same nitrogen taken together with the nitrogen form a 5-8 membered aromatic or non-aromatic ring having, in addition to the nitrogen, 0-2 ring heteroatoms selected from N, O, or S;

each R^{11} is independently selected from hydrogen, CO_2R^{12} ,
15 $CON(R^{12})_2$, OR^{12} , or a substituted or unsubstituted C_{1-8} aliphatic group;

each R^{12} is independently selected from a substituted or unsubstituted C_{1-8} aliphatic group; and

R^{14} is hydrogen, C_{1-8} aliphatic, C_{6-10} aryl, heteroaryl, C_{7-12}
20 aralkyl, heteroaralkyl, heterocyclyl, or R^3 and R^{14} taken together with their intervening nitrogens form a substituted or unsubstituted, aromatic or non-aromatic, 4-14 membered monocyclic, bicyclic or tricyclic ring system having, in addition to said intervening nitrogen, 0-4 ring
25 heteroatoms selected from nitrogen, sulfur or oxygen.

2. The compound of claim 1 wherein G is G1.

3. The compound of claim 2 having one or more features
30 selected from the group consisting of:

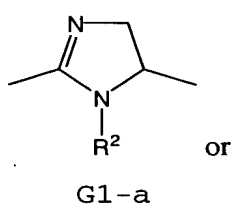
(a) X is oxygen;

(b) L_1 is a C_{2-3} alkylidene chain;

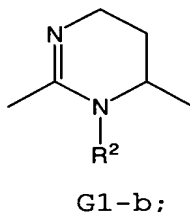
-114-

(c) Q is $-\text{CH}_2\text{CH}_2-$;

(d) G1 is G1-a or G1-b:



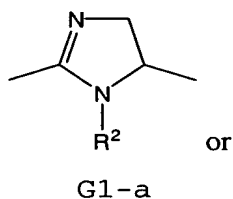
or



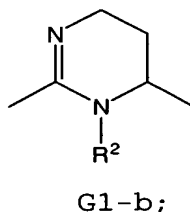
- 5 (e) R^4 and R^5 are each independently selected from a C_{1-4} aliphatic group or R^4 and R^5 taken together with their intervening nitrogen form a 5-6 membered ring;
- (f) Ring A is an optionally substituted phenyl or thienyl; and
- 10 (g) Ring B is a substituted phenyl or naphthyl.

4. The compound of claim 3 wherein:

- (a) X is oxygen;
- (b) L_1 is a C_{2-3} alkylidene chain;
- 15 (c) Q is $-\text{CH}_2\text{CH}_2-$;
- (d) G1 is G1-a or G1-b:



or



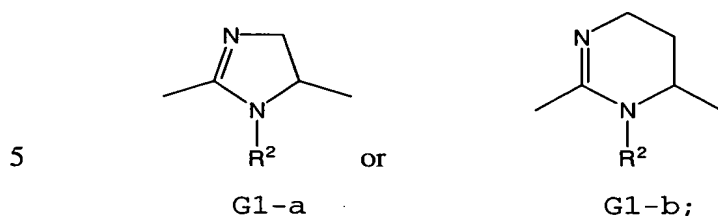
- (e) R^4 and R^5 are each independently selected from a C_{1-4} aliphatic group or R^4 and R^5 taken together with their intervening nitrogen form a 5-6 membered ring;
- 20 (f) Ring A is an optionally substituted phenyl or thienyl; and
- (g) Ring B is a substituted phenyl or naphthyl.

25

5. The compound of claim 2 having one or more features selected from the group consisting of:

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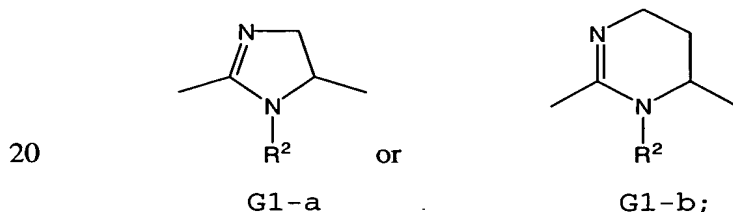
- (a) X is oxygen;
 (b) L₁ is -CH₂CH₂- or -CH₂CH₂CH₂-;
 (c) Q is -CH₂CH₂-;
 (d) G1 is G1-a or G1-b:



- (e) R⁴ and R⁵ are each independently selected from a C₁₋₃ aliphatic group or R⁴ and R⁵ taken together with their intervening nitrogen form a piperidinyl, pyrrolidinyl, piperazinyl or morpholinyl ring;
 10 (f) Ring A is an optionally substituted phenyl or thienyl;
 and
 (g) Ring B is a substituted phenyl or naphthyl.

15 6. The compound of claim 2 wherein:

- (a) X is oxygen;
 (b) L₁ is -CH₂CH₂- or -CH₂CH₂CH₂-;
 (c) Q is -CH₂CH₂-;
 (d) G1 is G1-a or G1-b:



- (e) R⁴ and R⁵ are each independently selected from a C₁₋₃ aliphatic group or R⁴ and R⁵ taken together with their intervening nitrogen form a piperidinyl, pyrrolidinyl, piperazinyl or morpholinyl ring;
 25 (f) Ring A is an optionally substituted phenyl or thienyl;
 and

(g) Ring B is a substituted phenyl or naphthyl.

7. The compound of claim 1 wherein G is G2.

5 8. The compound of claim 7 having one or more features selected from the group consisting of:

(a) X is oxygen;

(b) L₂ is a C₃₋₄ alkylidene chain;

(c) Q is -CH₂CH₂-;

10 (d) (i) R⁴ and R⁵ are each independently selected from a C₁₋₄ aliphatic group, or (ii) R⁴ and R⁵ taken together with their intervening nitrogen form a 5-6 membered ring, or (iii) R⁵ is a C₁₋₄ aliphatic group and R⁴ is aryl, aralkyl, heteroaryl, or heteroaralkyl;

15 (e) Ring A is an optionally substituted phenyl or thienyl; and

(f) Ring B is a substituted phenyl or naphthyl.

9. The compound of claim 7 wherein:

20 (a) X is oxygen;

(b) L₂ is a C₃₋₄ alkylidene chain;

(c) Q is -CH₂CH₂-;

(d) (i) R⁴ and R⁵ are each independently selected from a C₁₋₄ aliphatic group, or (ii) R⁴ and R⁵ taken together with
25 their intervening nitrogen form a 5-6 membered ring, or (iii) R⁵ is a C₁₋₄ aliphatic group and R⁴ is aryl, aralkyl, heteroaryl, or heteroaralkyl;

(e) Ring A is phenyl or thienyl; and

(f) Ring B is phenyl or naphthyl.

30

10. The compound of claim 7 having one or more features selected from the group consisting of:

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- (a) X is oxygen;
(b) L₂ is -CH₂CH₂CH₂- or -CH(CH₃)CH₂CH₂-;
(c) Q is -CH₂CH₂-;
(d) R⁴ and R⁵ are each independently selected from a C₁₋₃
5 aliphatic group or R⁴ and R⁵ taken together with their
intervening nitrogen form a piperidinyl, pyrrolidinyl,
piperazinyl or morpholinyl ring;
(e) Ring A is an optionally substituted phenyl or thienyl;
and
10 (f) Ring B is a substituted phenyl or naphthyl.

11. The compound of claim 7 wherein:

- (a) X is oxygen;
(b) L₂ is -CH₂CH₂CH₂- or -CH(CH₃)CH₂CH₂-;
15 (c) Q is -CH₂CH₂-;
(d) R⁴ and R⁵ are each independently selected from a C₁₋₃
aliphatic group or R⁴ and R⁵ taken together with their
intervening nitrogen form a piperidinyl, pyrrolidinyl,
piperazinyl or morpholinyl ring;
20 (e) Ring A is an optionally substituted phenyl or thienyl;
and
(f) Ring B is a substituted phenyl or naphthyl.

12. The compound of claim 1 wherein G is G3.

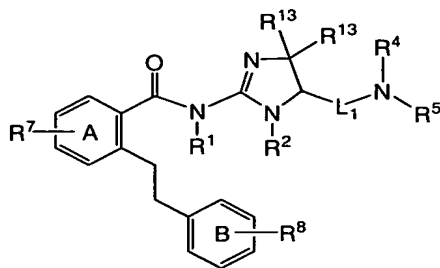
25

13. The compound of claim 12 having one or more features
selected from the group consisting of:

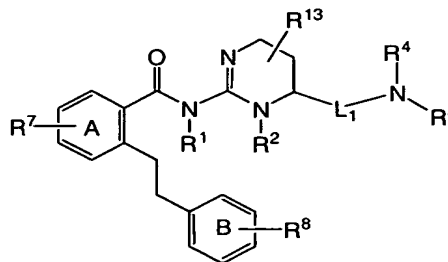
- (a) X is oxygen;
(b) L₃ is selected from a direct link, -CH₂-, -CH(R⁶)-,
30 -CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-;
(c) Q is -CH₂CH₂-;

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- (d) R^6 is C_{1-3} alkyl, CO_2H , $CO_2(C_{1-6}$ alkyl), CH_2CO_2H , or $CH_2CO_2(C_{1-6}$ alkyl);
- (e) R^{14} is selected from a C_{1-6} aliphatic group or a 5-6 membered heterocyclic ring;
- 5 (f) Ring A is an optionally substituted phenyl or thienyl; and
- (g) Ring B is a substituted phenyl or naphthyl.
14. The compound of claim 12 having one or more features selected from the group consisting of:
- (a) X is oxygen;
- (b) L_3 is $-CH_2-$ or $-CH(R^6)-$;
- (c) R^6 is C_{1-3} alkyl, CO_2H , $CO_2(C_{1-6}$ alkyl), CH_2CO_2H , or $CH_2CO_2(C_{1-6}$ alkyl);
- 15 (d) R^{14} is a 5-6 membered heterocyclic ring having a ring nitrogen and 0-1 additional ring heteroatoms selected from N, O or S;
- (e) Q is $-CH_2CH_2-$;
- (f) Ring A is an optionally substituted phenyl or thienyl;
- 20 and
- (g) Ring B is a substituted phenyl or naphthyl.
15. The compound of claim 1 represented by formulae II-A, II-B, II-C or II-D:

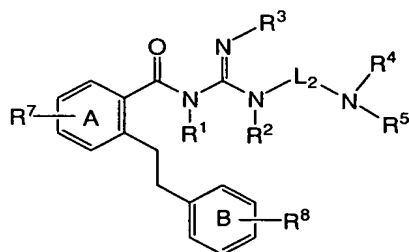


II-A

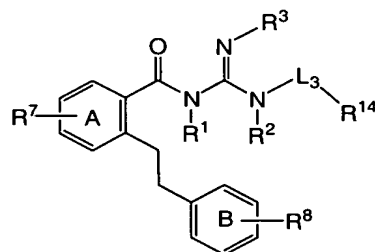


II-B

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II-C



or

II-D

5 wherein:

R^1 and R^2 are each hydrogen;

R^3 is hydrogen;

L_1 is $-\text{CH}_2\text{CH}_2-$ or $-\text{CH}_2\text{CH}_2\text{CH}_2-$;

L_2 is $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$, or

10 $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2-$;

L_3 is a direct link, $-\text{CH}_2-$, $-\text{CH}(\text{R}^6)-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, or $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$;

R^6 is C_{1-3} alkyl, CO_2H , $\text{CO}_2(\text{C}_{1-6}$ alkyl), $\text{CH}_2\text{CO}_2\text{H}$, or $\text{CH}_2\text{CO}_2(\text{C}_{1-6}$ alkyl);

15 R^7 is absent or is $-\text{halo}$, $-\text{NO}_2$, $-\text{CN}$, $-\text{R}^{12}$, $-\text{OR}^1$, $-\text{SR}^{12}$, $-\text{C}_{6-10}$ aryl, $-\text{heterocyclyl}$, $-\text{heteroaryl}$, $-(\text{C}_{6-10}$ aryl)alkyl,

$-(\text{heterocyclyl})\text{alkyl}$, $-(\text{heteroaryl})\text{alkyl}$, $-\text{N}(\text{R}^{10})_2$, $-\text{NR}^{10}\text{C}(\text{O})\text{R}^1$, $-\text{NR}^{10}\text{C}(\text{O})\text{N}(\text{R}^{10})_2$, $-\text{NR}^{10}\text{CO}_2\text{R}^{12}$, $-\text{CO}_2\text{R}^1$, $-\text{C}(\text{O})\text{R}^1$, $-\text{C}(\text{O})\text{N}(\text{R}^{10})_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^{10})_2$, $-\text{S}(\text{O})_2\text{R}^{12}$, $-\text{SO}_2\text{N}(\text{R}^{10})_2$, $-\text{S}(\text{O})\text{R}^{12}$,

20 $-\text{NR}^{10}\text{SO}_2\text{N}(\text{R}^{10})_2$, $-\text{NR}^{10}\text{SO}_2\text{R}^{12}$, or $-\text{C}(=\text{NH})-\text{N}(\text{R}^{10})_2$, or two adjacent R^7 taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

25 R^8 is $-\text{halo}$, $-\text{NO}_2$, $-\text{CN}$, or a substituted or unsubstituted group selected from $-\text{R}^{12}$, $-\text{OR}^1$, $-\text{SR}^{12}$, $-\text{C}_{6-10}$ aryl, $-\text{heterocyclyl}$, $-\text{heteroaryl}$, $-(\text{C}_{6-10}$ aryl)alkyl, $-(\text{heterocyclyl})\text{alkyl}$, $-(\text{heteroaryl})\text{alkyl}$, $-\text{N}(\text{R}^{10})_2$,

-NR¹⁰C(O)R¹, -NR¹⁰C(O)N(R¹⁰)₂, -NR¹⁰CO₂R¹², -CO₂R¹, -C(O)R¹,
-C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -S(O)₂R¹², -SO₂N(R¹⁰)₂, -S(O)R¹²,
-NR¹⁰SO₂N(R¹⁰)₂, -NR¹⁰SO₂R¹², or -C(=NH)-N(R¹⁰)₂, or two
adjacent R⁸ taken together with their intervening atoms
5 form a 5-6 membered unsaturated or partially unsaturated
ring having 0-2 heteroatoms selected from nitrogen, oxygen
or sulfur;

R⁴ and R⁵ (i) are each independently selected from a C₁₋₄
aliphatic group, or (ii) R⁴ and R⁵ taken together with
10 their intervening nitrogen form a 5-6 membered ring, or
(iii) R⁴ is a C₁₋₄ aliphatic group and R⁵ is aryl, aralkyl,
heteroaryl, or heteroaralkyl;

R¹⁴ is a C₁₋₆ aliphatic or 5-6 membered heterocyclic ring or R³
and R¹⁴ taken together with their intervening nitrogens
15 form a 4-6 membered ring;

each R¹³ is independently selected from hydrogen, C₁₋₆
aliphatic, or a substituent selected from the group
consisting of COR¹, CO₂R¹, CN, -N(R₁₀)₂, CON(R¹⁰)₂, -OR¹, or
two R¹³ on the same carbon taken together form =O, or two
20 R¹³ taken together with their intervening atoms form a 3-7
membered ring having 0-2 ring heteroatoms;

each R¹⁰ is independently selected from hydrogen, a
substituted or unsubstituted C₁₋₈ aliphatic group, C(=O)R¹,
CO₂R¹, SO₂R¹, or two R¹⁰ on the same nitrogen taken together
25 with the nitrogen form a 5-8 membered aromatic or non-
aromatic ring having, in addition to the nitrogen, 0-2
ring heteroatoms selected from N, O, or S;

each R¹¹ is independently selected from hydrogen or an
optionally substituted C₁₋₈ aliphatic group; and

30 each R¹² is independently selected from a substituted or
unsubstituted C₁₋₈ aliphatic group.

16. The compound of claim 15 wherein:

R¹ and R² are each hydrogen;

R³ is hydrogen;

L₁ is -CH₂CH₂- or -CH₂CH₂CH₂-;

5 L₂ is -CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH(CH₃)CH₂CH₂-, or
-CH(CH₃)CH₂CH₂CH₂-;

L₃ is a direct link, -CH₂-, -CH(R⁶)-, -CH₂CH₂-, -CH₂CH₂CH₂-, or
-CH₂CH₂CH₂CH₂-;

R⁶ is CO₂H, CO₂(C₁₋₆ alkyl), CH₂CO₂H, or CH₂CO₂(C₁₋₆ alkyl);

10 R⁷ is absent or is -halo, -CN, -R¹², -OR¹, -SR¹², -N(R¹⁰)₂,
-NR¹⁰C(O)R¹, -NR¹⁰C(O)N(R¹⁰)₂, -NR¹⁰CO₂R¹², -CO₂R¹, -C(O)R¹,
-C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -S(O)₂R¹², -SO₂N(R¹⁰)₂, -S(O)R¹²,
-NR¹⁰SO₂N(R¹⁰)₂, or -NR¹⁰SO₂R¹²;

R⁸ is -halo, -CN, or a substituted or unsubstituted group
15 selected from -R¹², -OR¹, -SR¹², , -N(R¹⁰)₂, -NR¹⁰C(O)R¹,
-NR¹⁰CO₂R¹², -CO₂R¹, -C(O)R¹, -C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂,
-S(O)₂R¹², -SO₂N(R¹⁰)₂, -S(O)R¹², -NR¹⁰SO₂N(R¹⁰)₂, or
-NR¹⁰SO₂R¹², or two adjacent R⁸ taken together with their
intervening atoms form a 5-6 membered unsaturated or
20 partially unsaturated ring having 0-2 heteroatoms selected
from nitrogen, oxygen or sulfur;

R⁴ and R⁵ are each independently selected from C₁₋₃ alkyl or R⁴
and R⁵ taken together with their intervening nitrogen form
a 5-6 membered ring;

25 R¹⁴ is a C₁₋₆ aliphatic or a 5-6 membered heterocyclic ring
having a ring nitrogen and 0-1 additional ring heteroatoms
selected from N, O or S;

each R¹³ is hydrogen;

each R¹⁰ is hydrogen;

30 each R¹¹ is independently selected from hydrogen or an
optionally substituted C₁₋₅ aliphatic group; and

each R^{12} is independently selected from a substituted or unsubstituted C_{1-5} aliphatic group.

17. The compound of claim 16 wherein:

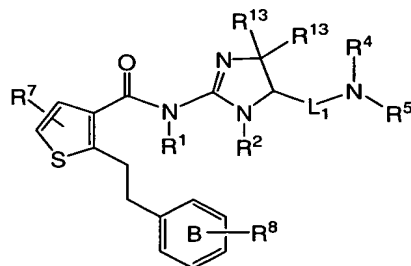
5 R^7 is absent or is halo;

Ring B is a phenyl ring having two R^8 substituents that are para to one another or Ring B is a naphthyl ring; and

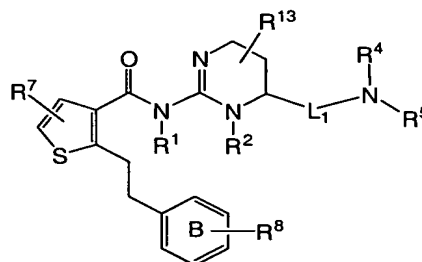
each R^8 is independently selected from halo, C_{1-4} alkyl, C_{1-3} alkoxy, $CO(C_{1-3}$ alkyl), $CONH(C_{1-3}$ alkyl), $SO_2(C_{1-3}$ alkyl), or

10 $SO_2NH(C_{1-3}$ alkyl).

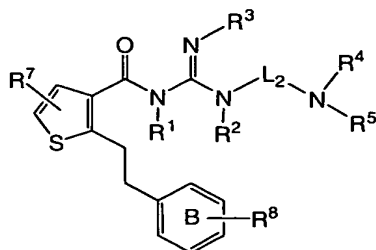
18. The compound of claim 1 represented by formulae III-A, III-B, III-C or III-D:



15 III-A

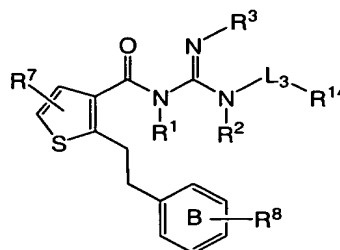


III-B



III-C

or



III-D

20 wherein:

R^1 , and R^2 are each hydrogen;

R^3 is hydrogen;

L_1 is $-\text{CH}_2\text{CH}_2-$ or $-\text{CH}_2\text{CH}_2\text{CH}_2-$;

L_2 is $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$, or
 $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2-$;

L_3 is a direct link, $-\text{CH}_2-$, or $-\text{CH}_2\text{CH}_2-$;

5 R^7 is absent or is $-\text{halo}$, $-\text{CO}_2\text{R}^1$, $-\text{C}(\text{O})\text{R}^1$, $-\text{C}(\text{O})\text{N}(\text{R}^{10})_2$, or two adjacent R^7 taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

10 R^8 is $-\text{halo}$, $-\text{NO}_2$, $-\text{CN}$, or a substituted or unsubstituted group selected from $-\text{R}^{12}$, $-\text{OR}^1$, $-\text{SR}^{12}$, $-\text{C}_{6-10}$ aryl, $-\text{heterocyclyl}$, $-\text{heteroaryl}$, $-(\text{C}_{6-10} \text{ aryl})\text{alkyl}$, $-(\text{heterocyclyl})\text{alkyl}$, $-(\text{heteroaryl})\text{alkyl}$, $-\text{N}(\text{R}^{10})_2$, $-\text{NR}^{10}\text{C}(\text{O})\text{R}^1$, $-\text{NR}^{10}\text{C}(\text{O})\text{N}(\text{R}^{10})_2$, $-\text{NR}^{10}\text{CO}_2\text{R}^{12}$, $-\text{CO}_2\text{R}^1$, $-\text{C}(\text{O})\text{R}^1$,
15 $-\text{C}(\text{O})\text{N}(\text{R}^{10})_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^{10})_2$, $-\text{S}(\text{O})_2\text{R}^{12}$, $-\text{SO}_2\text{N}(\text{R}^{10})_2$, $-\text{S}(\text{O})\text{R}^{12}$, $-\text{NR}^{10}\text{SO}_2\text{N}(\text{R}^{10})_2$, $-\text{NR}^{10}\text{SO}_2\text{R}^{12}$, or $-\text{C}(=\text{NH})-\text{N}(\text{R}^{10})_2$, or two adjacent R^8 taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen
20 or sulfur;

R^4 and R^5 are each independently selected from C_{1-3} alkyl or R^4 and R^5 taken together with their intervening nitrogen form a 5-6 membered ring;

R^{14} is a C_{1-6} aliphatic or a 5-6 membered heterocyclic ring
25 having a ring nitrogen and 0-1 additional ring heteroatoms selected from N, O or S;

each R^{13} is independently selected from hydrogen, C_{1-6} aliphatic, or a substituent selected from the group consisting of COR^1 , CO_2R^1 , CN , $-\text{N}(\text{R}^{10})_2$, $\text{CON}(\text{R}^{10})_2$, $-\text{OR}^1$, or
30 two R^{13} on the same carbon taken together form $=\text{O}$, or two R^{13} taken together with their intervening atoms form a 3-7 membered ring having 0-2 ring heteroatoms;

each R¹⁰ is independently selected from hydrogen, a substituted or unsubstituted C₁₋₈ aliphatic group, C(=O)R¹, CO₂R¹, SO₂R¹, or two R¹⁰ on the same nitrogen taken together with the nitrogen form a 5-8 membered aromatic or non-aromatic ring having, in addition to the nitrogen, 0-2 ring heteroatoms selected from N, O, or S;

5 each R¹¹ is independently selected from hydrogen or an optionally substituted C₁₋₈ aliphatic group; and each R¹² is independently selected from a substituted or unsubstituted C₁₋₈ aliphatic group.

10

19. The compound of claim 18 wherein:

R¹, R², and R³ are each hydrogen;

L₁ is -CH₂CH₂- or -CH₂CH₂CH₂-;

15 L₂ is -CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH(CH₃)CH₂CH₂-, or -CH(CH₃)CH₂CH₂CH₂-;

L₃ is a direct link, -CH₂-, or -CH₂CH₂-;

R⁷ is absent;

R⁸ is -halo, -CN, or a substituted or unsubstituted group selected from -R¹², -OR¹, -SR¹², , -N(R¹⁰)₂, -NR¹⁰C(O)R¹, -NR¹⁰CO₂R¹², -CO₂R¹, -C(O)R¹, -C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -S(O)₂R¹², -SO₂N(R¹⁰)₂, -S(O)R¹², -NR¹⁰SO₂N(R¹⁰)₂, or -NR¹⁰SO₂R¹², or two adjacent R⁸ taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

20

25

R⁴ and R⁵ are each independently selected from C₁₋₃ alkyl or R⁴ and R⁵ taken together with their intervening nitrogen form a 5-6 membered ring;

30 R¹⁴ is a C₁₋₆ aliphatic or a 5-6 membered heterocyclic ring having a ring nitrogen and 0-1 additional ring heteroatoms selected from N, O or S;

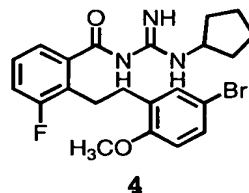
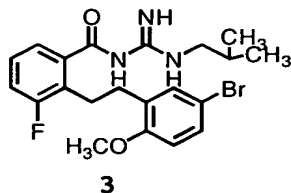
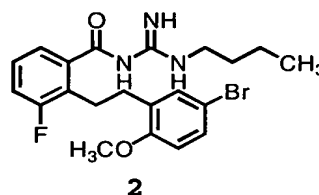
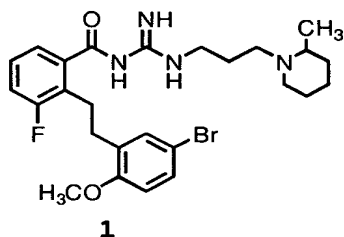
-125-

- each R^{13} is hydrogen;
each R^{10} is hydrogen;
each R^{11} is independently selected from hydrogen or an
optionally substituted C_{1-5} aliphatic group; and
5 each R^{12} is independently selected from a substituted or
unsubstituted C_{1-5} aliphatic group.

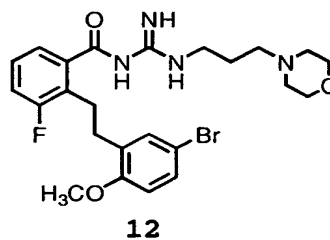
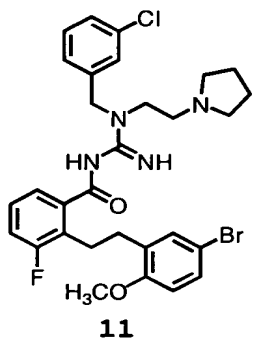
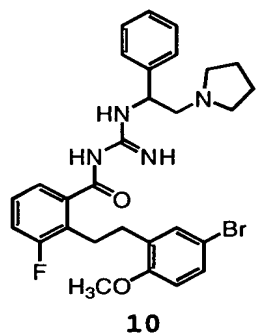
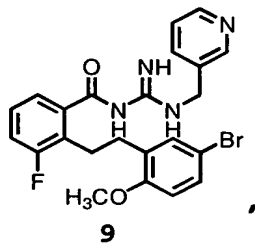
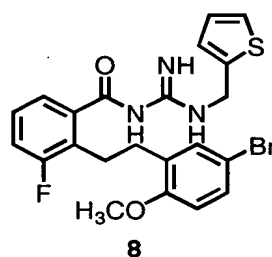
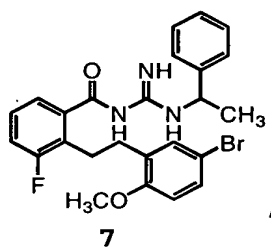
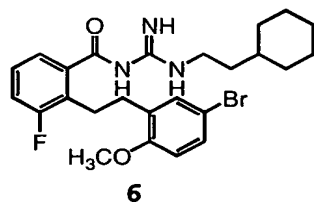
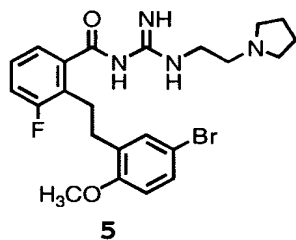
20. The compound of claim 18 wherein:

- Ring B is a phenyl ring having two R^8 substituents that are
10 para to one another or Ring B is a naphthyl ring; and
Each R^8 is independently selected from halo, C_{1-4} alkyl, C_{1-3}
alkoxy, $CO(C_{1-3}$ alkyl), $CONH(C_{1-3}$ alkyl), $SO_2(C_{1-3}$ alkyl), or
 $SO_2NH(C_{1-3}$ alkyl).

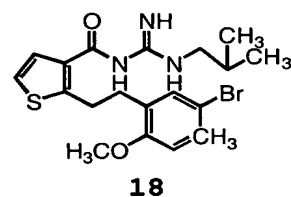
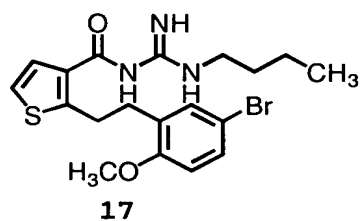
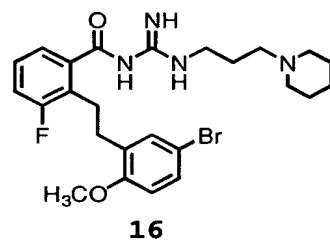
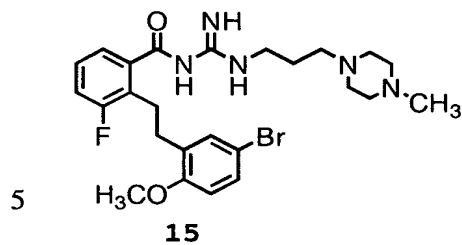
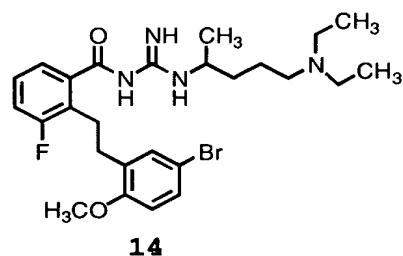
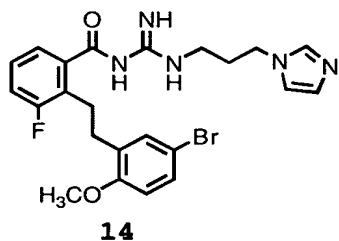
- 15 21. A compound selected from the group consisting of: ✓



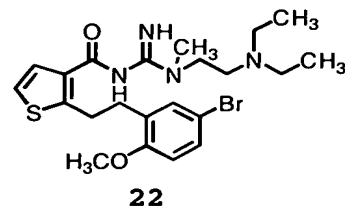
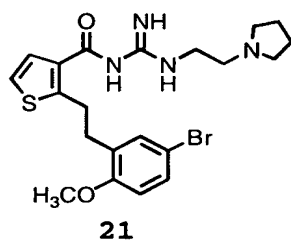
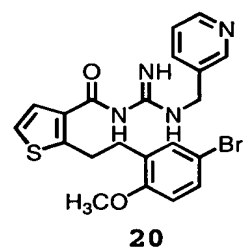
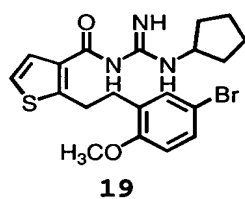
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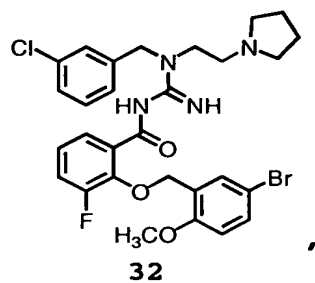
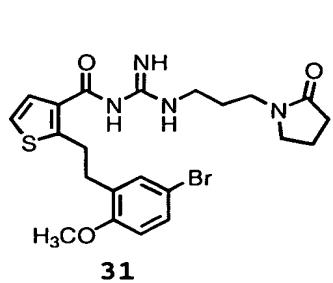
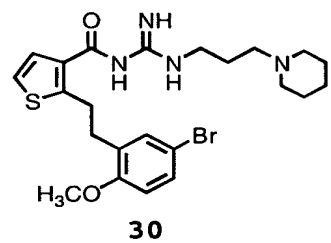
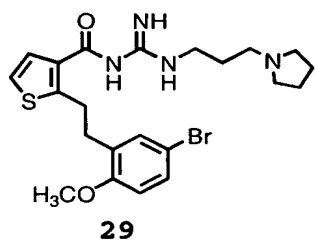
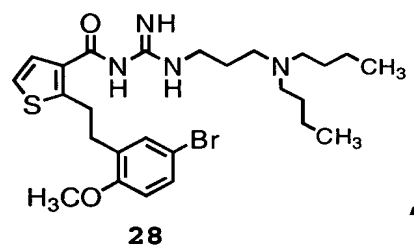
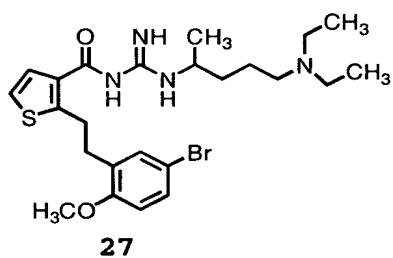
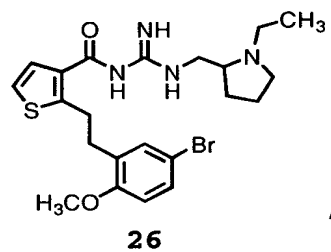
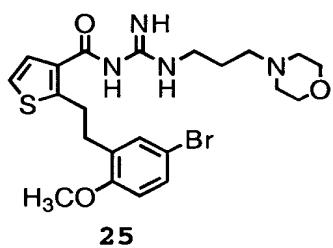
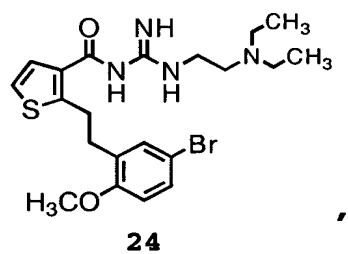
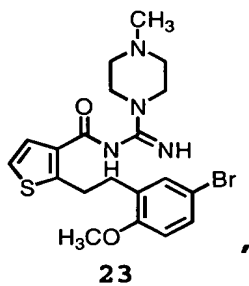
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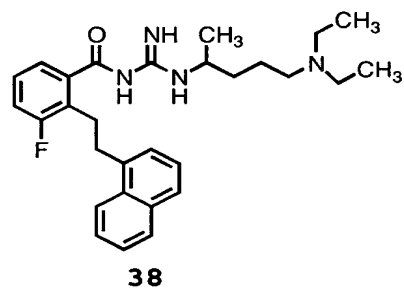
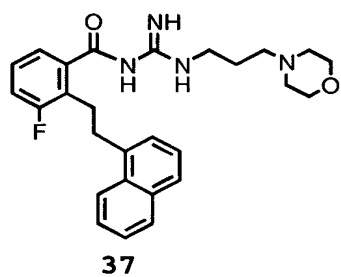
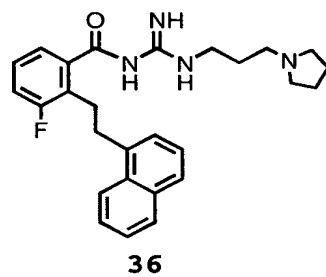
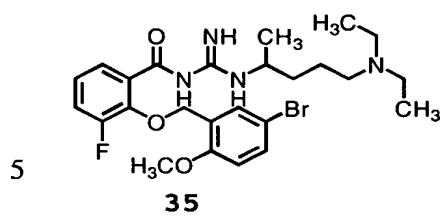
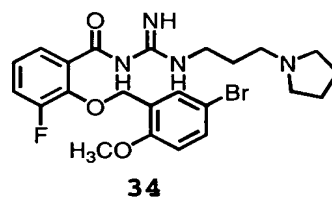
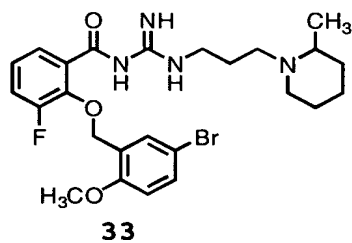


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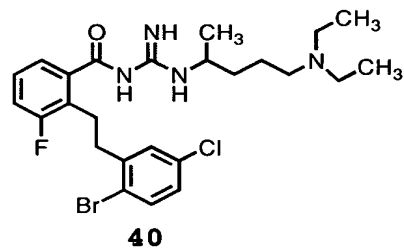
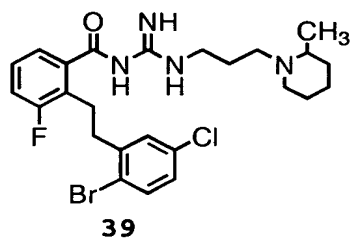


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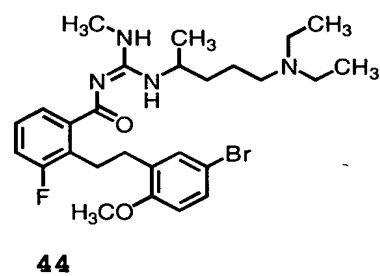
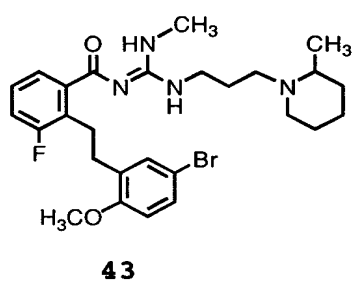
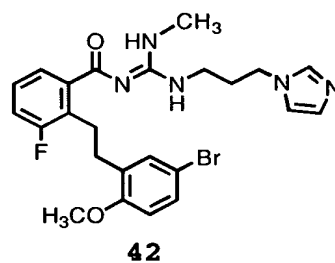
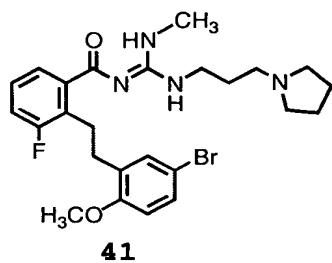




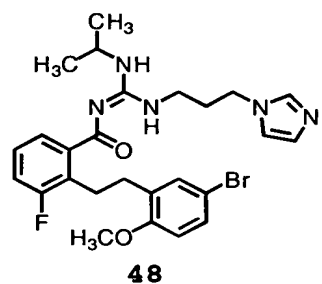
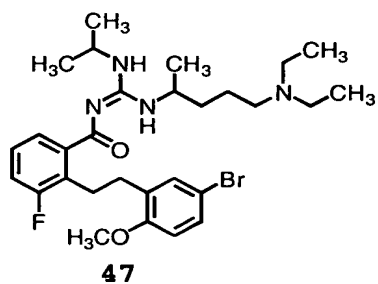
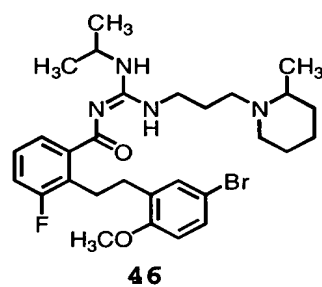
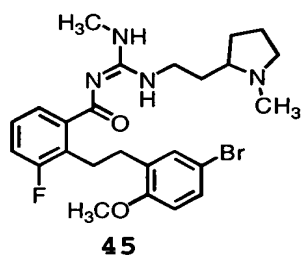
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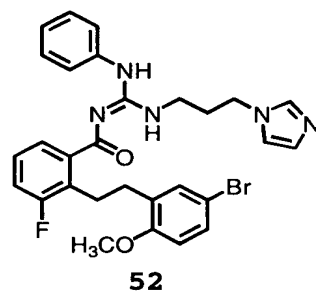
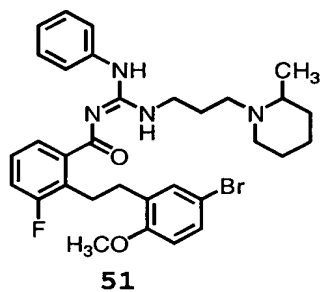
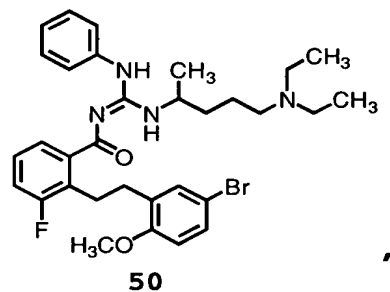
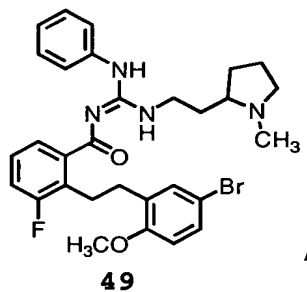


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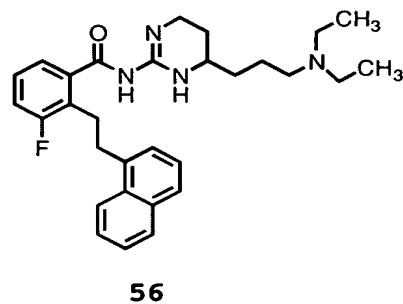
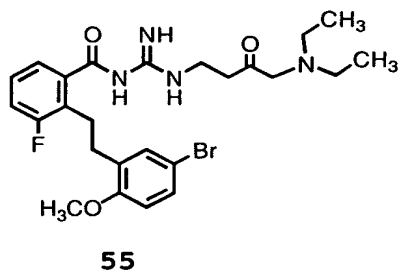
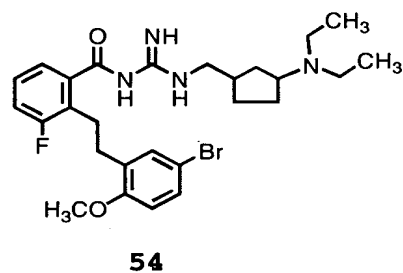
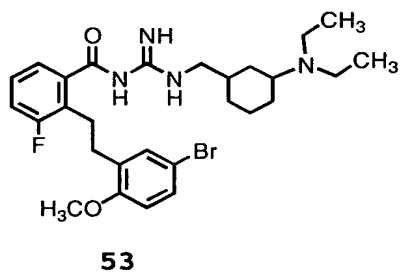


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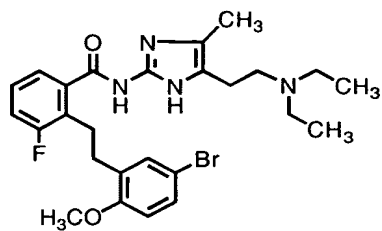
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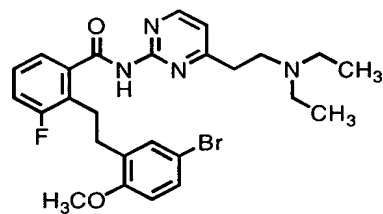
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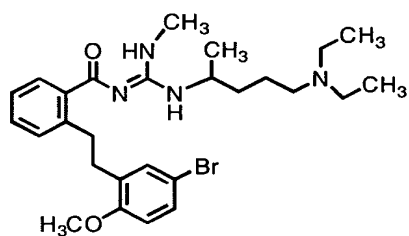
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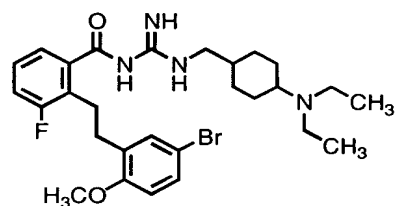
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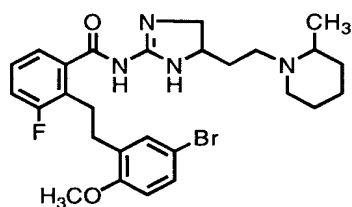
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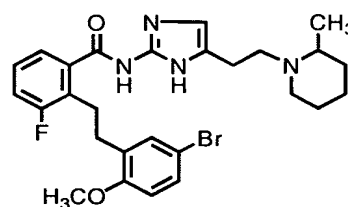
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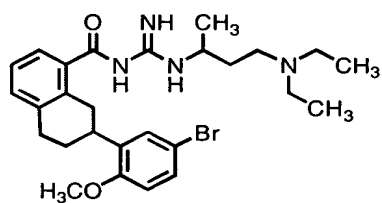
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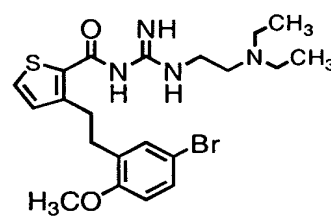
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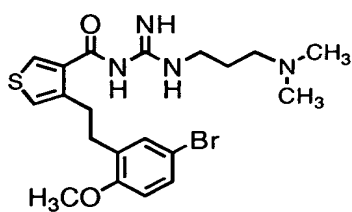
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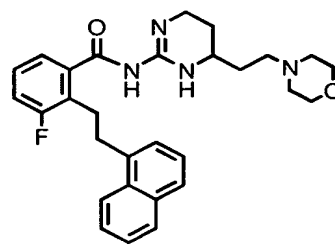
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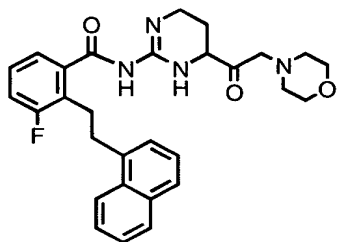
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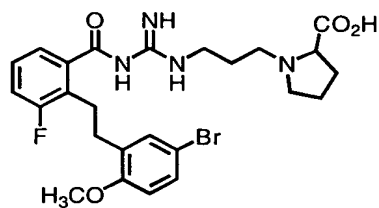
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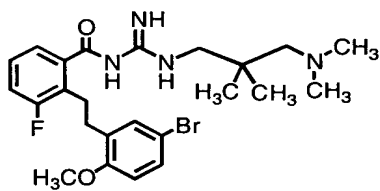
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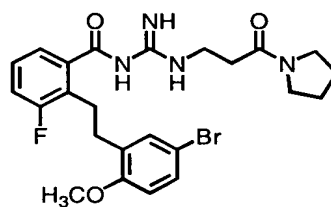
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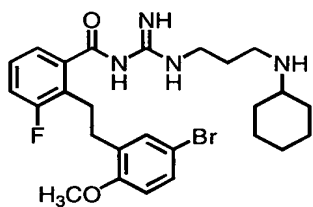
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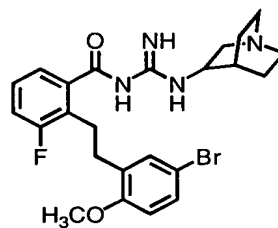
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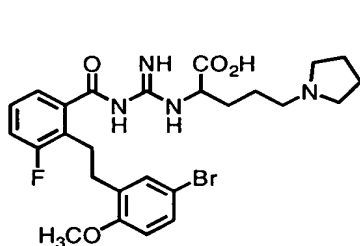
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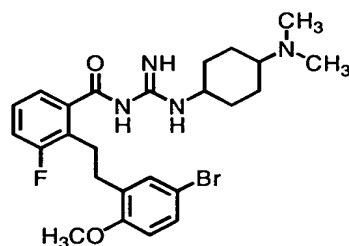
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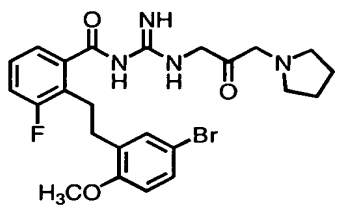
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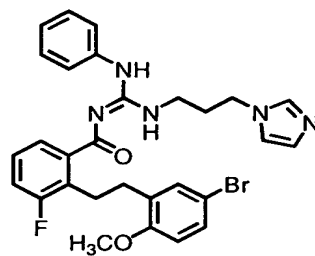
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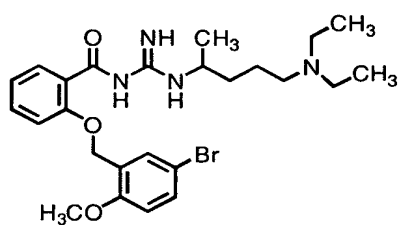
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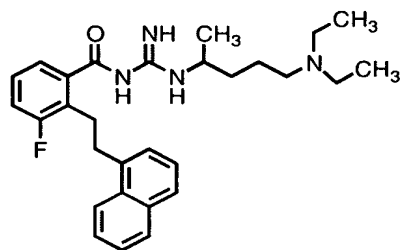
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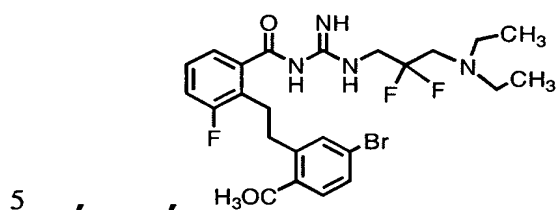
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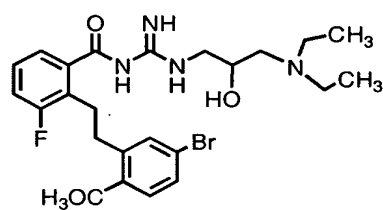
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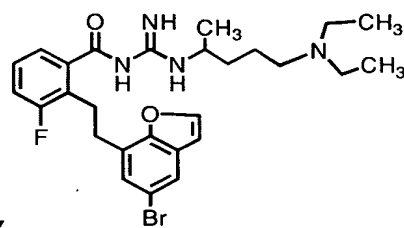
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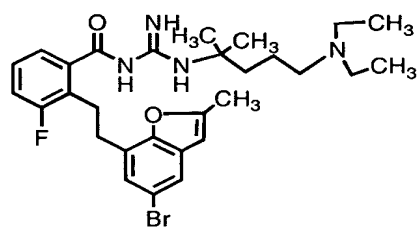
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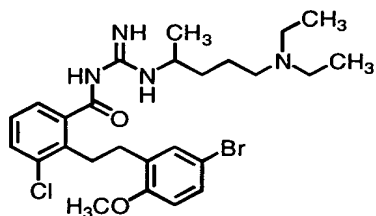


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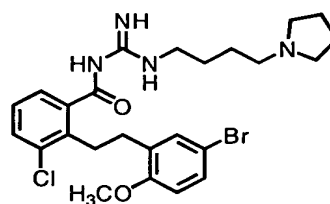


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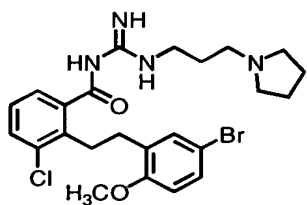
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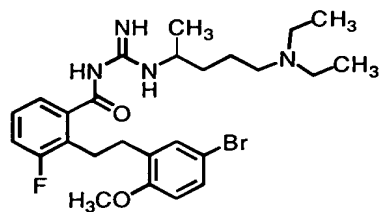
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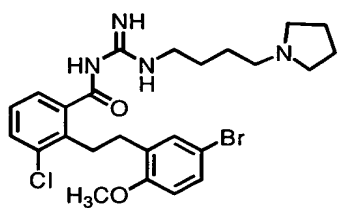


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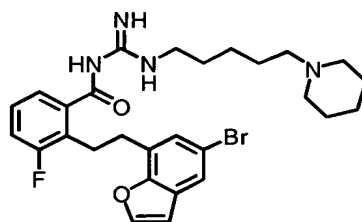


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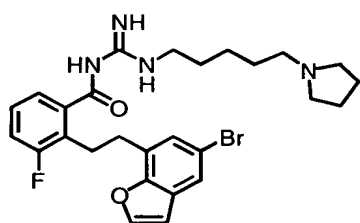
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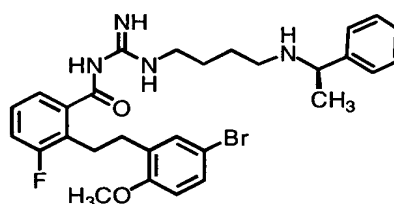
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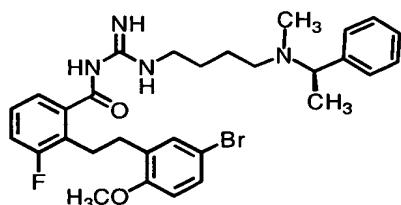
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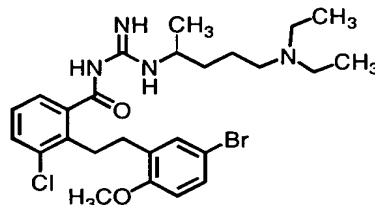
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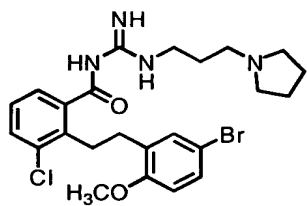
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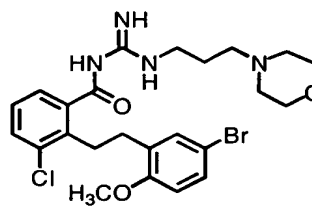
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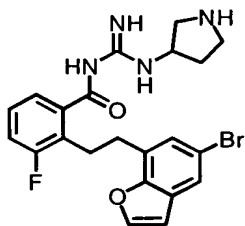
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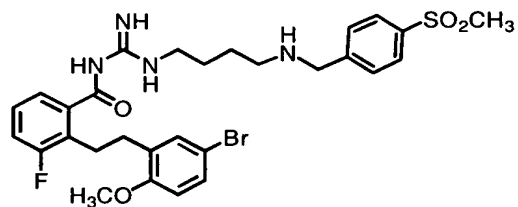
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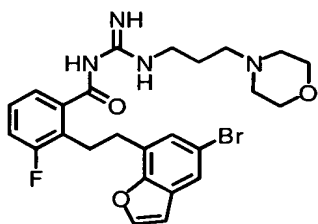
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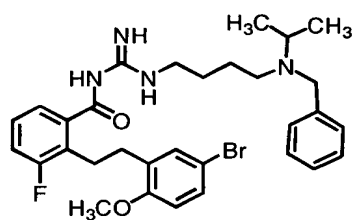
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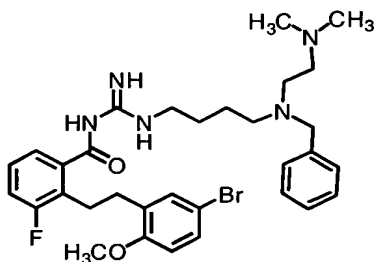
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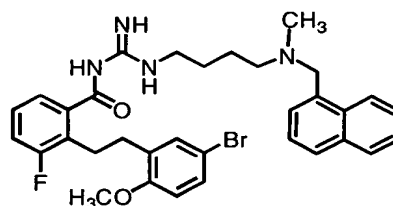
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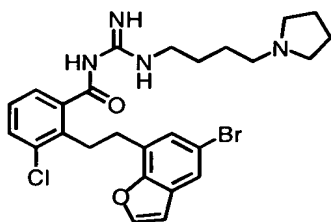
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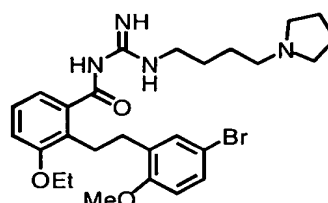
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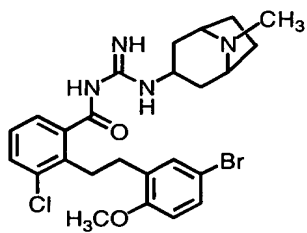
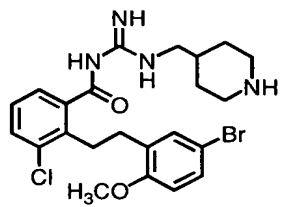
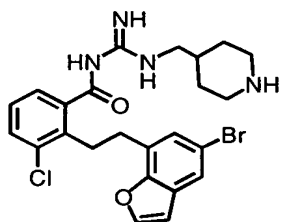
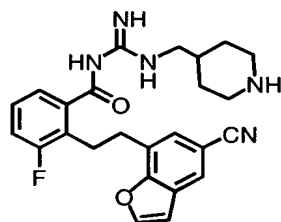
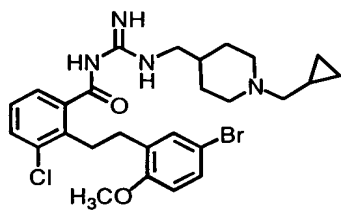
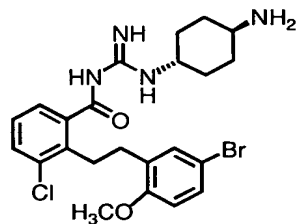
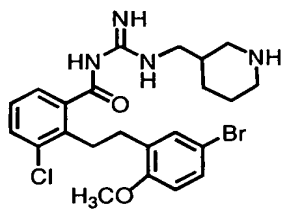
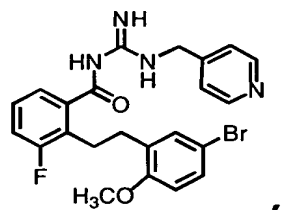


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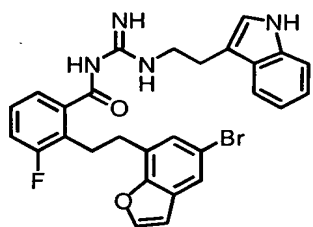
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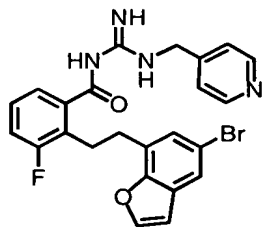
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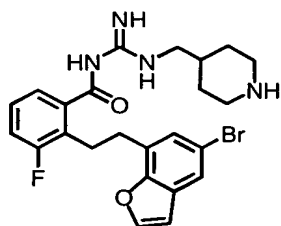
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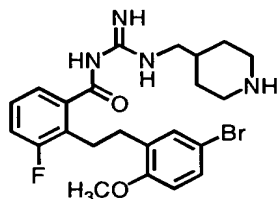
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112

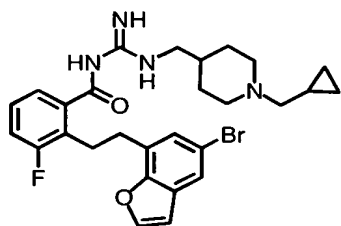


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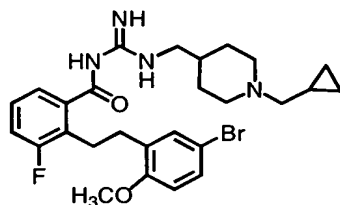


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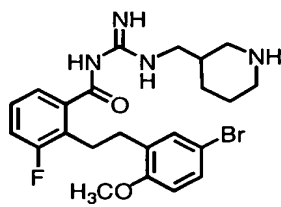
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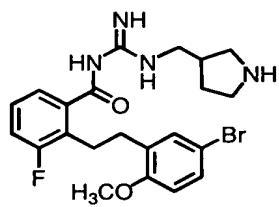
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116



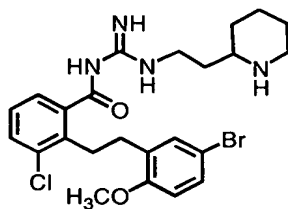
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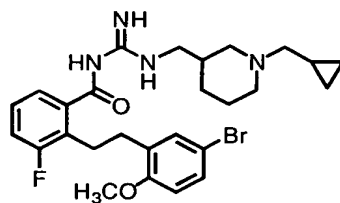
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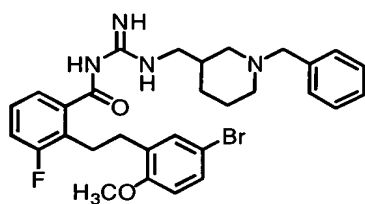
-139-



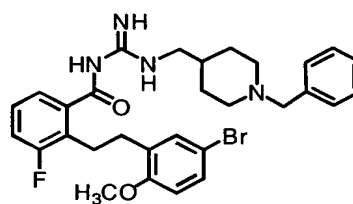
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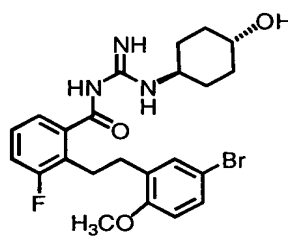
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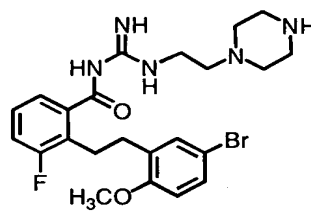
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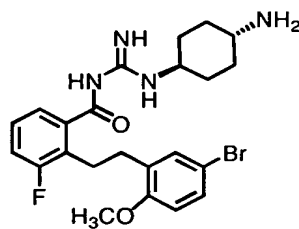
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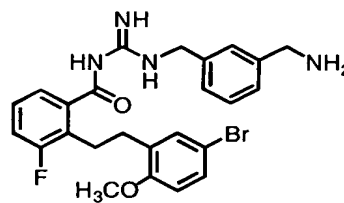
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124

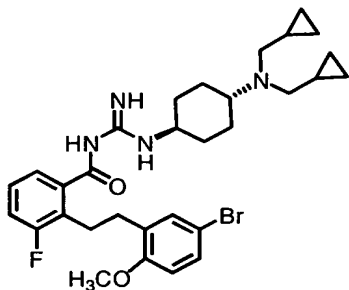
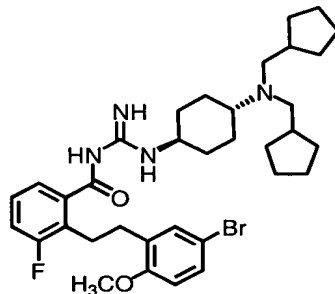
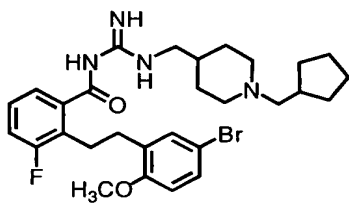
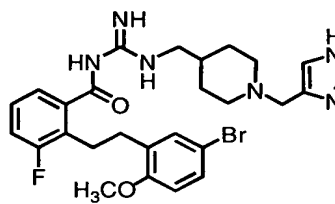
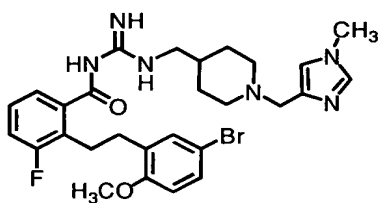
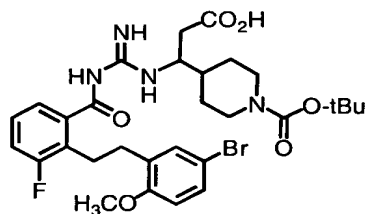
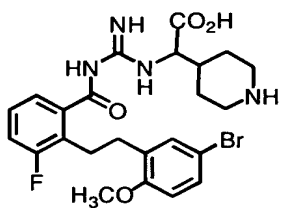
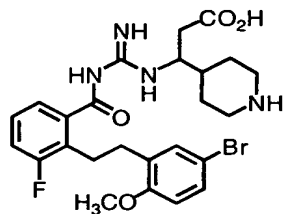


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126

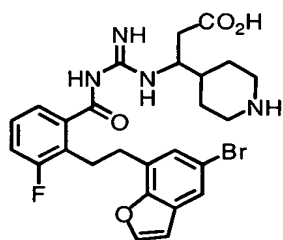
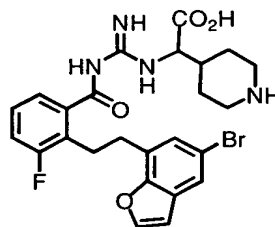
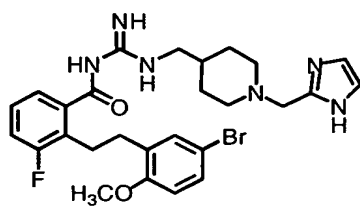
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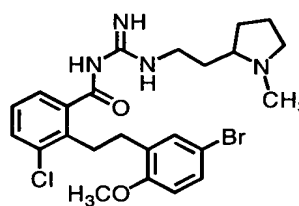
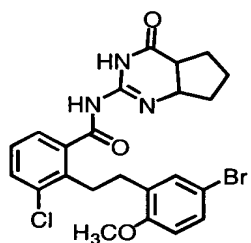
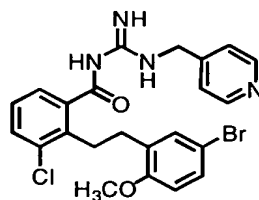
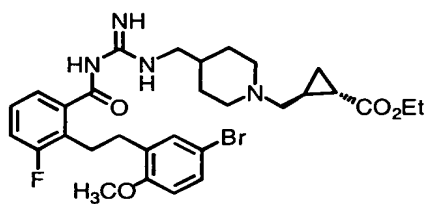
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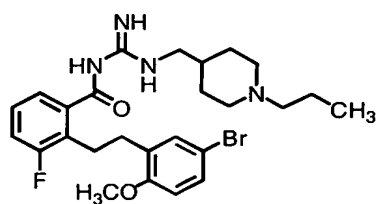
-141-

**135****136****137**

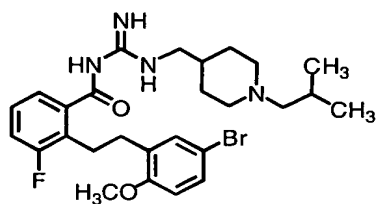
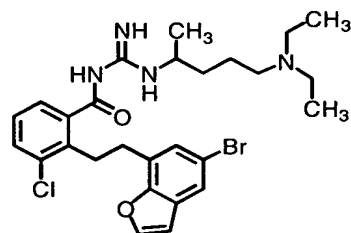
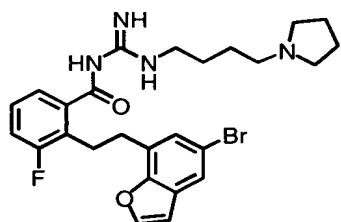
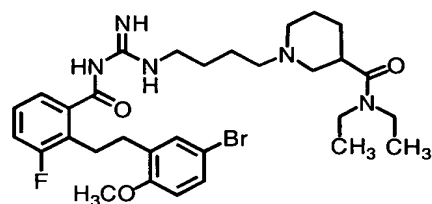
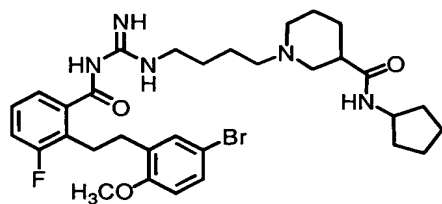
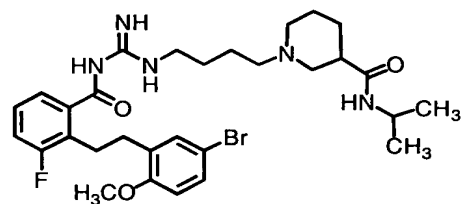
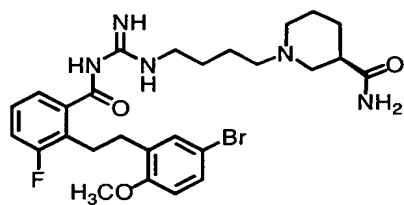
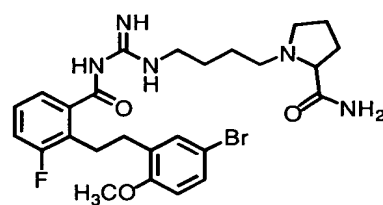
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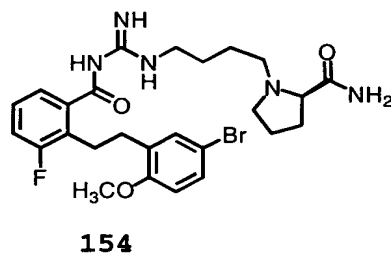
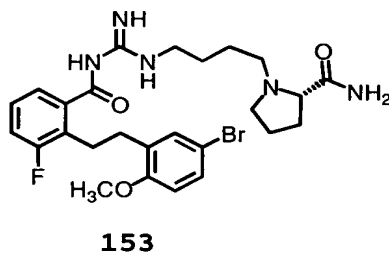
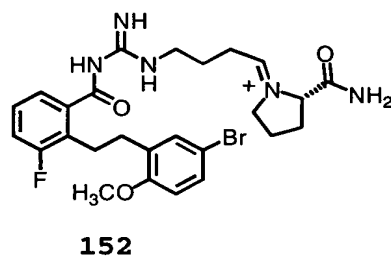
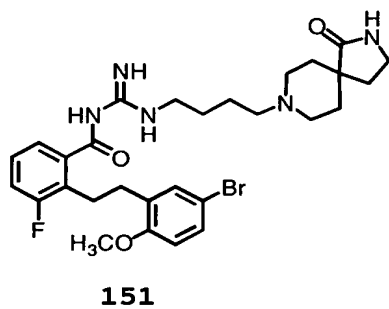
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**142**

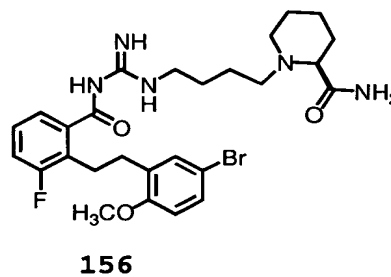
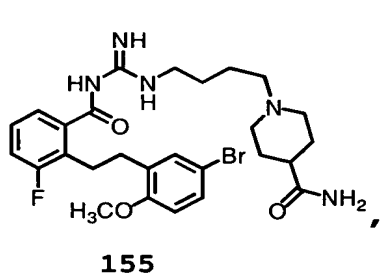
-142-

**143****144****145****146****147****148****149****150**

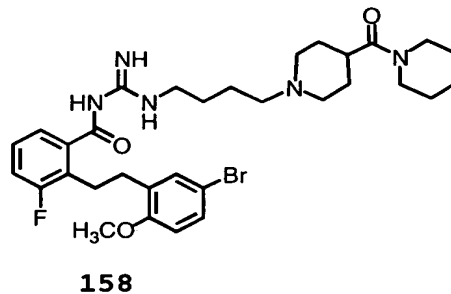
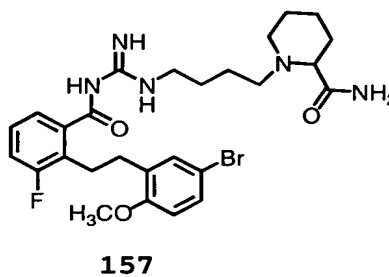
-143-



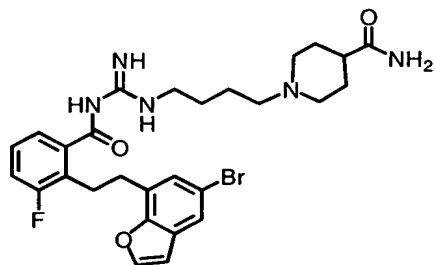
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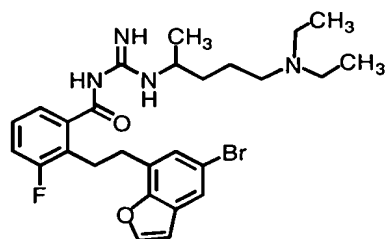
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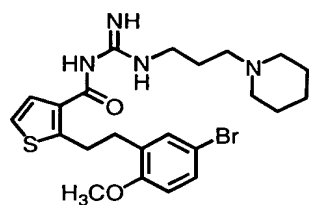
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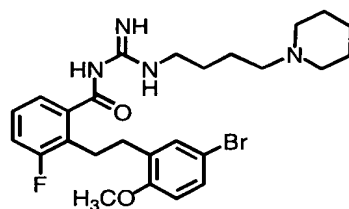


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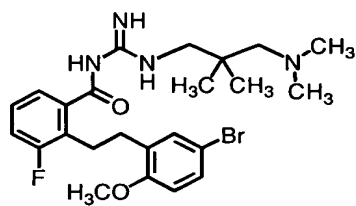


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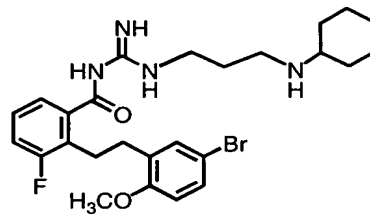
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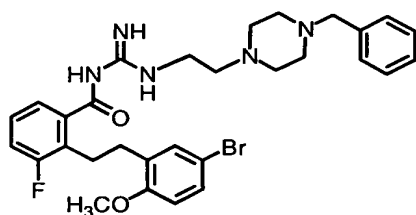
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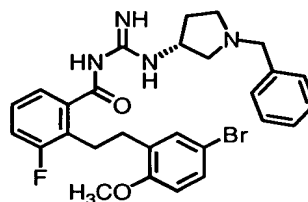


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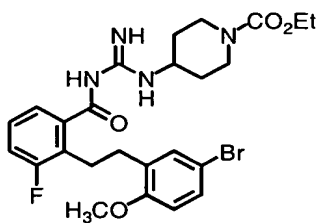
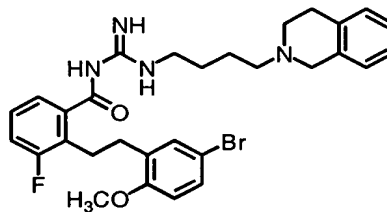
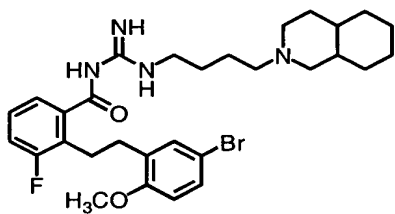
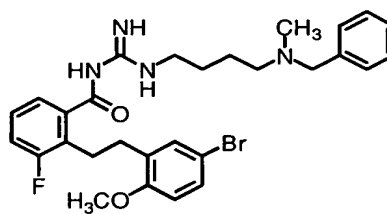
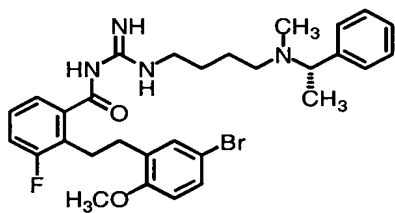
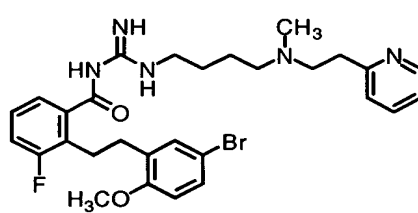
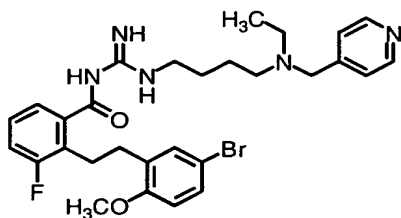
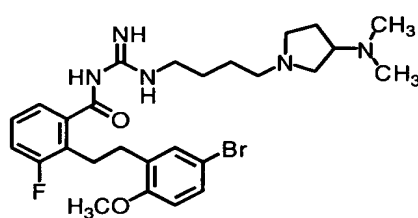
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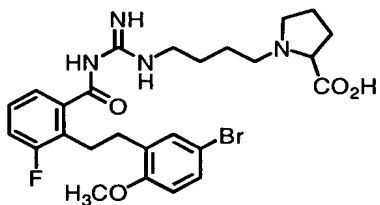


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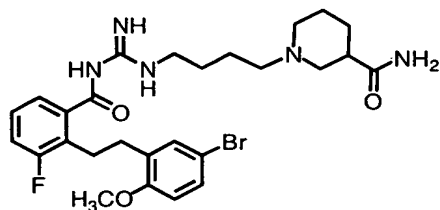
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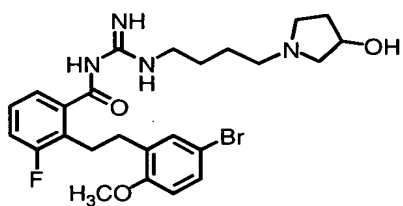
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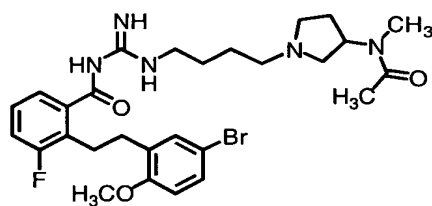
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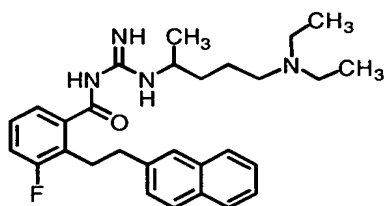
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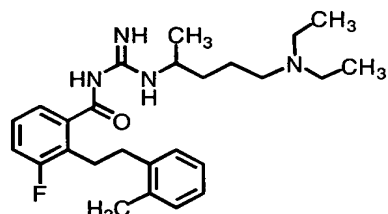
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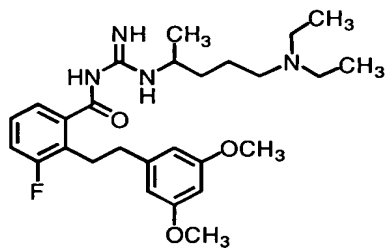
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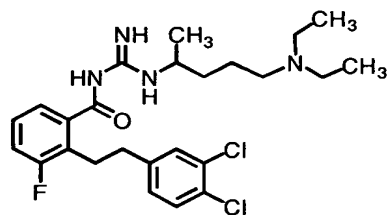
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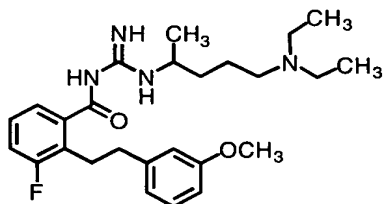
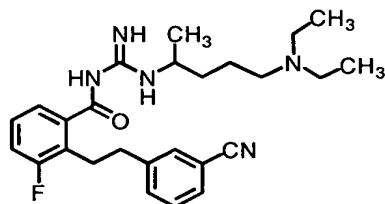
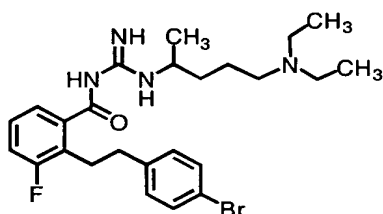
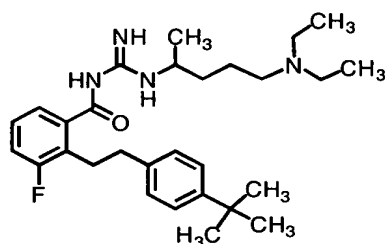
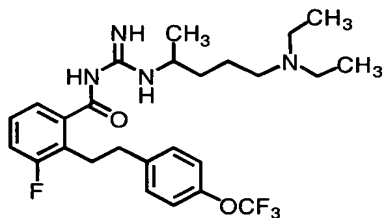


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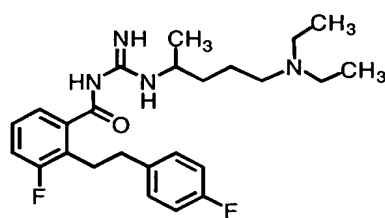
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**183****184****185****186****187**

, and

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10

22. A pharmaceutical composition comprising a compound according to claim 1 and a pharmaceutically acceptable carrier.

15

23. A method of treating an MC4-R associated disorder in a patient in need thereof comprising administering to said patient a compound of formula (I) in claim 1.

20

24. A method of treating an MC4-R associated disorder in a patient in need thereof comprising administering to said

patient a pharmaceutical composition comprising a compound of formula (I) in claim 1.

25. A method of treating a weight loss disorder in a subject
5 identified as in need of such treatment comprising
administering a compound of formula (I) in claim 1.

26. The method of claim 25, wherein the weight loss disorder
is a cachexia, aging involuntary weight loss, catabolic
10 wasting, or anorexia.

27. The method of claim 26, wherein cachexia is cancer
cachexia, cardiac cachexia, chronic illness cachexia, or AIDS
cachexia.
15

28. A method of treating a bone associated disorder in a
subject identified as in need of such treatment comprising
administering a compound of formula (I) in claim 1.

20 29. The method of claim 28, wherein the bone associated
disorder is osteoporosis, bone fractures, bone formation
associated with surgical procedures, osteogenesis imperfecta,
hypophosphatasia, Paget's disease, fibrous dysplasia,
osteopetrosis, myeloma bone disease, or the depletion of
25 calcium in bone.

30. A method of treating a pain disorder in a subject
identified as in need of such treatment comprising
administering a compound of formula (I) in claim 1.
30

31. The method of claim 30, wherein the neuronal disorder is
neuropathic pain or allodynia.

32. A method of inhibiting MC4-R activity in a patient in
need thereof comprising administering to said patient a
pharmaceutical composition comprising a compound of formula
5 (I) in claim 1.